Heitzmann (6) & Abbott (7)

CONTRIBUTIONS TO THE KNOWLEDGE OF TUMORS OF THE JAWS.

By CARL HEITZMANN, M.D., AND FRANK ABBOTT, M.D.

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Modern histologists agree that the animal body is composed of only four varieties of tissues,—viz., connective, muscle, nerve, and epithelial. All attempts at basing a nomenclature of tumors on strictly anatomical or histological grounds must be in agreement with this division of the normal tissues. In fact, there is not a single morbid growth to be found which does not have a representation in some physiological tissue. Among the four varieties, it is only the connective that carries blood and lymph-vessels. Muscle-fibers and epithelia are destitute of vessels, they being supplied with nourishment by the surrounding and subjacent layers of connective tissue, or rather the vessels therein contained.

The nerve-fibers are surrounded by vascularized connective tissue, while the gray substance of the nerve-centers is considerably mixed with it, although a satisfactory distinction between the gray substance and this tissue—the so-called neuroglia—has never been made. The normal connective tissue in its perfect development appears in four varieties,—viz., the myxomatous, the fibrous, the cartilaginous, and the osseous. In accord with this subdivison, we find a number of varieties of tumors which are composed entirely of a myxomatous, fibrous, cartilaginous, or bony tissue, being termed myxoma, fibroma, chondroma, and osteoma. These are the representatives of a type of tumors known clinically as benign, since they grow very slowly, do not cause pain, do not ulcerate except after local injuries, and do not produce secondary tumors in internal organs, and even after many years' growth never cause death directly.

Fat-tissue is a sub-variety of myxomatous, and tumors largely composed of such tissue are termed lipoma. If blood or lymph-

vessels are largely prevailing in a tumor, it is called vascular, or angioma. If muscles enter the structure of the tumor we speak of it as a myoma, and if nerve-fibers are present in great numbers the designation is neuroma.

In all these instances more or less fibrous connective tissue (the carrier of blood-vessels) enters into the architecture of the tumor, and even in certain varieties of angioma, the so-called cavernous—the fibrous connective tissue bounding the caverns filled with venous blood—carry, as a rule, capillary blood-vessels. According to the prevailing structure present, we will designate a given tumor as a myo-fibroma if the muscle-tissue predominates, or fibro-myoma if the fibrous connective tissue is in excess over the muscle-tissue. Here again we have four typical varieties of tumors, which we call benign from a clinical point of view.

The unripe or embryonal condition of all forms of connective tissue is termed indifferent or medullary. Tumors that are built up of such tissue belong, as Virchow has shown many years ago, to the group of connective-tissue tumors, for which he proposed the term sarcoma. These grow rapidly, causing more or less pain and sometimes ulceration, besides being very prone to excite the formation of secondary tumors in internal organs, thus directly leading to the death of the patient. Clinically they are known as malignant tumors. Since the term would indicate a fleshy tumor, we propose to abandon the name sarcoma and substitute for it the word myeloma, which really designates what the tumor is composed of, viz., medullary tissue.

It is impossible to tell why myeloma should possess deleterious properties, which enables it to transform all sorts of tissues and organs into its own peculiar structure. Neither do we understand the reason why myeloma appears mainly in children and young persons, in contradistinction to carcinoma, which is, in the great majority of cases, a disease of advanced life. The main constituents of myeloma are globular or spindle-shaped corpuscles, with very little intervening basis-substance. This feature furnishes the most important point for a differential diagnosis between the benign and malignant forms of tumors of the connective-tissue series. There are, however, transitional forms in which portions of the new growth are well supplied with basis-substance of any of the four above-named types; whereas other portions are composed mainly of medullary tissue. It also occurs that we meet in the middle of a benign tumor with nests of medullary corpuscles, usually in the neighborhood of the sources of nutrition,—*i. e.*, around the blood-vessels.

In compliance with our nomenclature, we shall designate tumors of such a mixed character as myxo-myeloma, fibro-myeloma, chondro-

myeloma, and osteo-myeloma. Combinations like these always mean a tumor growing rapidly, being prone to recur after operations not skillfully performed, and gradually to assume the characteristic features of purely malignant myeloma. In such cases attempts at eradication, such as cauterization and injuries of any nature, hasten the transformation of a slightly into a markedly malignant growth.

The fourth group of tissues, the epithelium, never produces a tumor alone, since it is invariably combined with more or less vascularized connective tissue. If the latter produces papillary elevations, covered on the outer surface with stratified epithelium, we term it a warty growth, or papilloma. If the epithelium produces acinous or tubular prolongations into the depth of the connective tissue, we have a glandular tumor, or adenoma. Both of these types are clinically benign; whereas the third type, in which epithelial and connective tissue are intermixed without any regularity, is designated cancer, or carcinoma, being decidedly malignant. Again we are unable to say wherein rests this pronounced capacity of carcinoma to infect all sorts of neighboring tissues, more especially the adjacent lymph-ganglia, and to transform normal tissues into its own.

Quite recently, however, Scheürlen, of Würtemberg, Germany, has demonstrated bacilli of a characteristic form and growth, which he claims are the elements which cause cancer. Schill, of Dresden, claims priority of this discovery, maintaining at the same time that bacilli similar to those of cancer are also to be found in sarcoma or myeloma. This discovery is too novel to admit of its immediate and unqualified acceptance, although there are good clinical reasons for the assumption that specific germs may be present in either of these diseases.

One large group of tumors is represented by closed cavities filled with liquid or semi-solid contents, the so-called cysts. Such growths arise mainly in organs which, in a physiological condition, contain epithelial or glandular structures. In many instances a new formation of glandular tissue (an adenoma) precedes the appearance of a cyst. Closed cavities, however, are not infrequently found in both benign and malignant types of connective-tissue tumors, and in such cases we are in the dark as to the origin of cysts, designating the new formation cysto-fibroma, cysto-osteoma, cysto-myeloma, etc.

As to the cause of tumors, we wish to allude to the theory of the late Cohnheim, which suggests misplaced embryonal germs. This brilliant theory was by himself subsequently limited to certain varieties, such as primary cancer in the bone or in lymph ganglia. Unfortunately, however, this theory cannot be proven, either by direct observation or by experiments upon animals. We are positive

of only one fact, viz., that an acute traumatism or oft-repeated slight injuries—in short, a local irritation—furnish in many instances the issue for the appearance of abnormal growths. In several of our specimens the trace of a previous traumatism was found under the microscope, in the shape of clusters of pigment, the result of a hemorrhage that must have occurred long before. Inflammation of the gum and the pericementum are acknowledged to be fertile sources of tumors, as well as traumatisms or other irritations.

Our observations are based upon seventeen different tumors. These embrace the most common types of both benign and malignant tumors of the jaws. The great majority were primary on the jaws, and only two cases, one of myeloma and one of carcinoma, are secondary to the jaws by contiguity. We exclude from our consideration all tumors of the teeth proper.

I.—Myxoma.

This variety of tumor is not rare on the gums around the teeth. The specimen under observation is the size of a robin's-egg, with a nodulated surface, originally of a blood-red color, of rather soft consistence, and grown upon the gum of the lower jaw, left side between the second bicuspid and first molar. It occurred at every pregnancy, for the third time, in the mouth of a lady aged about twenty-six years. Tumors had been removed from the same locality four different times, when the patient was a girl from twelve to fourteen years of age.

With low powers of the microscope the raspberry or papillary appearance was well marked upon the surface, as represented in Fig. 1. The surface is coated with a single row of columnar epithelium, which is bounded toward the subjacent connective tissue without distinctness,—so much so that the lowest portions of columnar epithelia and the bodies wedged in between them blend with the adjacent layers of medullary tissue. The so-called structureless layer can be made out in but few places. The main mass of the growth consists of an extremely delicate net-work of fibrous connective tissue with interspersed nuclei mainly at the points of intersection. The meshes of this net-work contain as a rule only one medullary corpuscle; but near the surface such corpuscles are present in large numbers, to such an extent that the reticulum is rendered invisible. The corpuscles are comparatively small and nearly compact near the periphery, while they are granular and markedly larger in the deeper portions. The outermost portions of the tumor, owing to the abundance of medullary corpuscles, have the character of a myeloma; but the gradual appearance of a myxomatous basis-substance in the deeper portions proves that the tissue is myxomatous, and the

clusters of the medullary corpuscles merely signify a rapid growth at the surface.

FIG. 1.

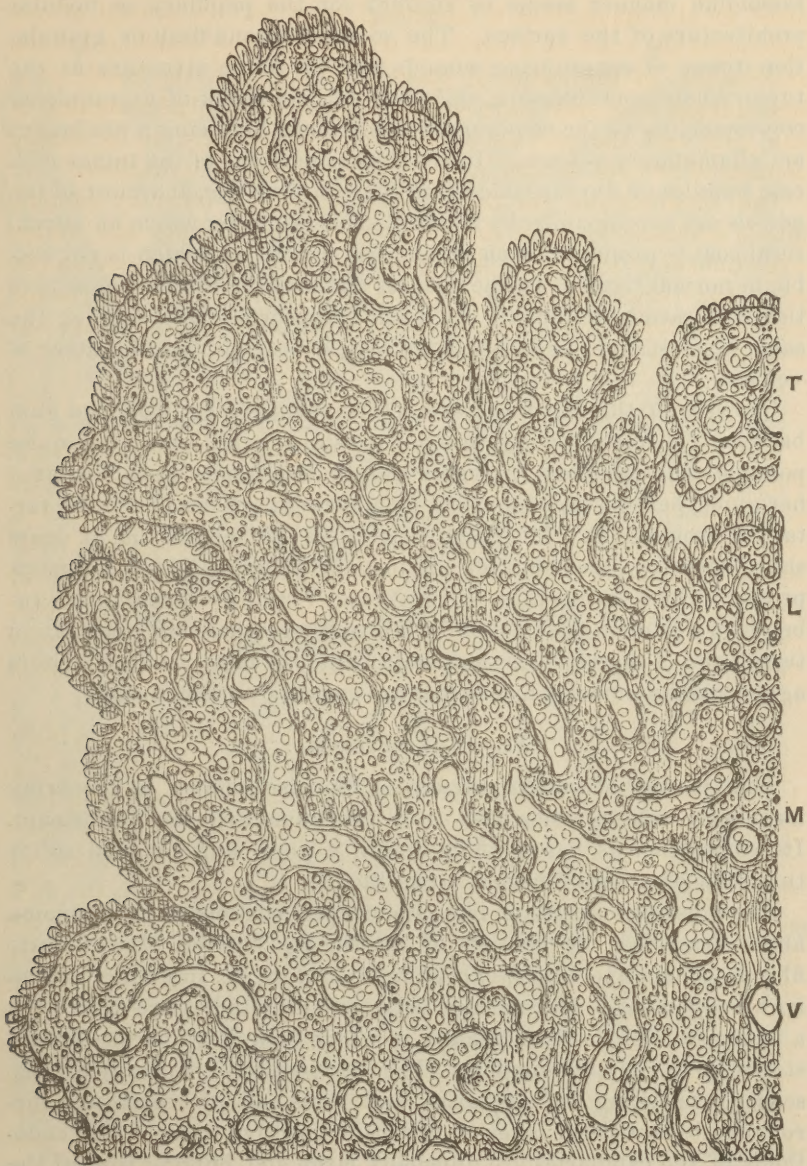

FIG. 1. Myxoma or Granuloma of the Gum of the Lower Jaw. L, Longitudinal; T, Transverse section of the papillæ on the surface; M, Myxomatous tissue; V, Blood-vessels traversing the myxomatous tissue. × 100.

A striking feature of this growth is the large number of wide capillary blood-vessels, which run mainly in a vertical direction to the

surface, and therefore appear in transverse sections where the papillæ are cut transversely. The arrangement of the capillaries in a tassel-like manner seems to account for the papillary or nodular architecture of the surface. The so-called proud-flesh or granulation tissue of suppurating wounds has the same structure as the tumor under consideration, and some authors speak of a granuloma corresponding to the structure of a myxoma, but being a product of an inflammatory process. In the deeper portions of the tumor delicate bundles of fibrous connective tissue are visible, and most of the vessels are accompanied by tracts of such tissue, by which an adventitial coat is produced, even around the capillaries, which is not visible in normal tissue. In the deepest portions the fibrous connective tissue is rather abundant, the medullary corpuscles being at the same time scanty, and the blood-vessels bearing the character of veins.

Growths of this kind are sometimes seen arising from the gum between the teeth, owing to some constant irritation. It is quite possible that the lady in whose mouth the tumor grew irritated her gums, perhaps mechanically, by allowing particles of food or tartar to accumulate. The microscope does not enable us to draw sharp boundary lines between products of inflammation and tumors proper. Good authorities—for instance, Virchow—claim that a tubercle or a gumma due to syphilis is a tumor composed of granulation tissue, and is therefore granulomata, whereas most modern writers agree that the nodules mentioned are caused by inflammation.

II.—Myxo-Fibroma.

This variety of benign tumors is likewise known as occurring frequently, taking issue both from the gums and the periosteum. Its consistence is harder than that of a pure myxoma, and softer than that of a pure fibroma. (See Fig. 2.)

The illustration is taken from the deepest portions of the myxoma above described. It consists of interlacing bundles of a delicate fibrous connective tissue, exhibiting therefore an indistinct reticular arrangement. The meshes between the bundles are filled with a finely-granular basis-substance, in which medullary corpuscles are stored up in varying numbers. The blood-vessels are comparatively scanty, consisting of capillaries and veins, all of which are surrounded by a distinct layer of fibrous connective tissue. The endothelia of the capillaries are unusually large and bulging toward the caliber. In some places the capillary appears to be surrounded by two or more endothelial layers, which add considerably to the thickness of the vascular wall. The specimen affords a good opportunity for the study of the manner in which, first, myxomatous arises from

medullary, and fibrous from myxomatous tissue, a process which, as is well known, is of frequent occurrence in the history of develop-

Fig. 2.

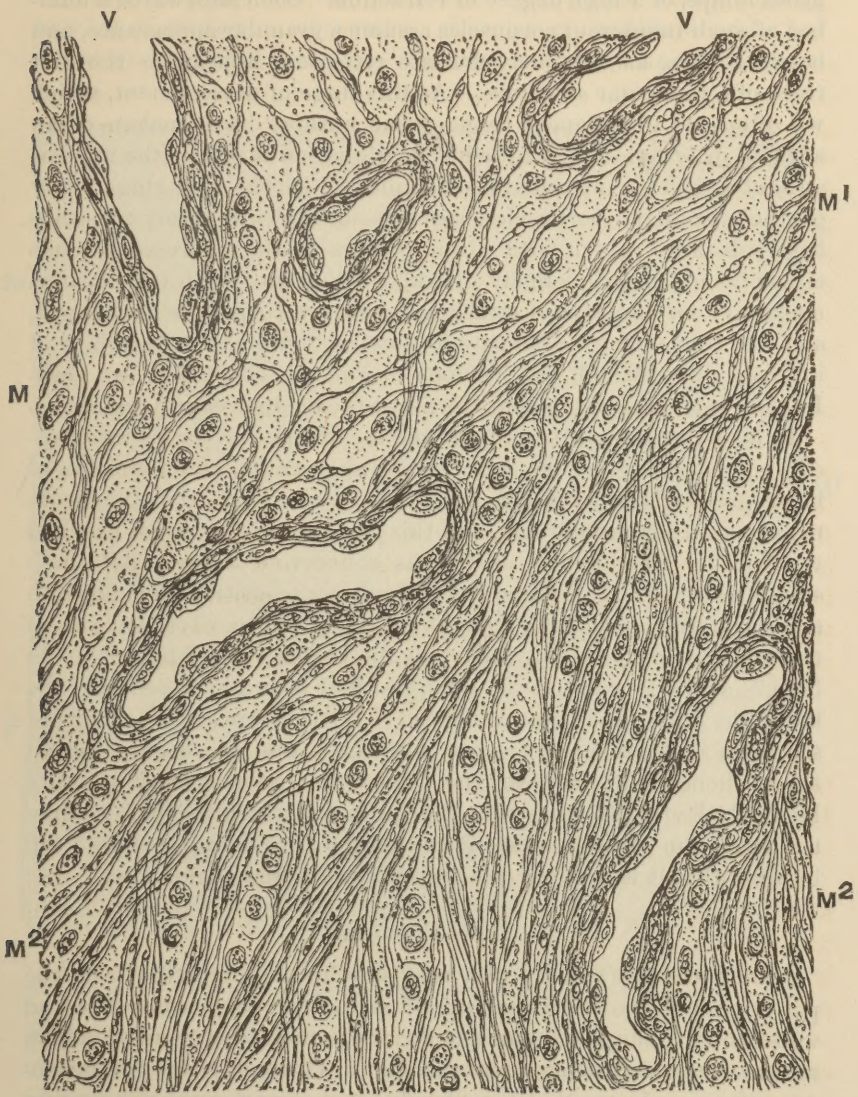

Fig. 2. Myxo-Fibroma of the Gum of the Lower Jaw. M, Myxomatous tissue, composed of delicate fibrous bundles; M 1, The bundles coarser still, exhibiting the reticular arrangement; M 2, The fibrous bundles, broad, inclosing fields of a myxomatous basis-substance; V, V, Large capillary blood-vessels. × 200.

ment of normal fibrous connective tissue. At first the tissue is apparently nothing but an aggregation of indifferent or medullary

corpuscles, the tissue nature of which is determined only by the fact that all corpuscles are united with one another by means of delicate threads. The corpuscles themselves are originally small homogeneous lumps, of a high degree of refraction. Soon afterwards a number of such indifferent corpuscles assume a granular appearance, and between them an extremely delicate reticulum appears as the first trace of a recticular structure. At this stage of development, which we often see in inflamed tissue, some authors have spoken of an adenoid or lymph-tissue, by which designation is meant the appearance of a delicate myxomatous reticulum. In the next stage many of the medullary corpuscles are transformed into a myxomatous basis-substance, which with lower powers of the microscope looks either homogeneous or finely granular. Fields of such transformed medullary corpuscles have either one or several corpuscles unchanged, and are bordered by a delicate fibrous recticulum, at the points of intersection, at which small oblong or globular corpuscles are seen. In this stage of development the tissue is called purely myxomatous.

If, by a further splitting up of the medullary corpuscles into delicate spindles, the fibrous reticulum is augmented, and the fields of myxomatous basis-substance narrowed, we have a transition from myxoma into myxo-fibroma, and this transition is the more marked the broader the bundles of fibrous connective tissue. All these stages, to be sure, cannot be traced in direct transition from one into another, but we conclude, from observing the successive portions of the same tumor, being medullary at the periphery and fibrous at its base, that the former are the youngest and least developed, and the latter the oldest and most advanced. With the previous theory of secretion of basis-substance, we were at a loss to account for all these phenomena; whereas the theory first advanced by the late Max Schultze (1861), known as the "transformation theory," renders the formation of basis-substance explicable, providing that we keep in mind that it is nothing but protoplasm altered chemically.

III.—Fibroma.

Solid and dense tumors of a very slow growth, starting from the periosteum of the jaw-bones, are of rather frequent occurrence and well known to surgeons. The name given to them was "epulis," which means a tumor growing upon the gum. Obviously this is a misnomer, since we know that tumors of this description take issue as a rule from the periosteum, and invade the gum in a rather secondary way. One of the striking features of such benign tumors is the presence of protoplasmic masses with a varying number of nuclei the so-called giant cells of previous pathologists. They are present in greatly varying numbers, mainly in that portion of the tumor

nearest the periosteum, often being arranged in groups, and lacking altogether in the peripheral portions of the growth. (See Fig. 3.) When such bodies are visible, as a rule they are surrounded by embryonal tissue, and it is easy to observe their origin from a varying number of medullary corpuscles. The latter coalesce, thereby losing their individual boundary lines, and produce a uniformly gran-

FIG. 3.

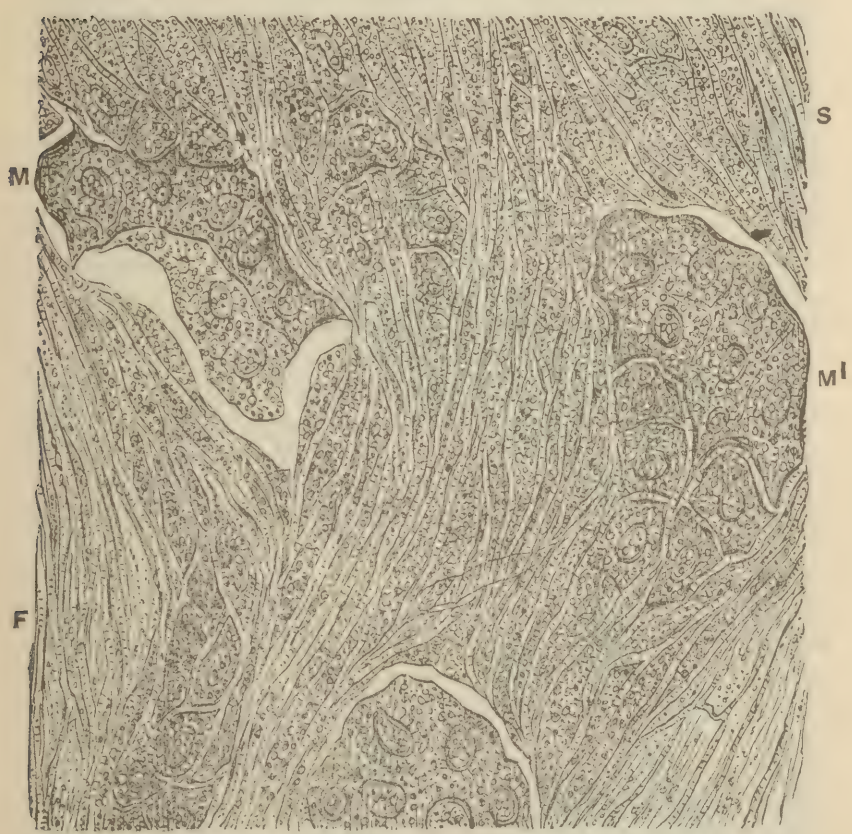

FIG. 3. Base of Fibroma with Multinuclear Bodies, so-called Giant Cells. S, Spindle shaped medullary corpuscles; F, Fibrous basis-substance having originated from spindle-shaped medullary corpuscles; M, Multinuclear body retracted from the surrounding medullary tissue; M 1, Multinuclear body in connection with large medullary or endothelial elements. × 600.

ular mass of protoplasm, in which we recognize either scattered nuclei or coarser granules, so called nucleoli. Around the corpuscle, which is often of irregular shape, sending offshoots into the neighboring medullary tissue, the adjacent medullary corpuscles produce a kind of capsule, between which and the multinuclear bodies a gap is not infrequently seen,—caused, as it were, by the shrinkage of the "giant cell." It is known that bodies of this description are often

met with in the normal medullary tissue of forming and growing bone. We often find them in those bay-like excavations that appear in the cementum and dentine of temporary teeth during the pro-

FIG. 4.

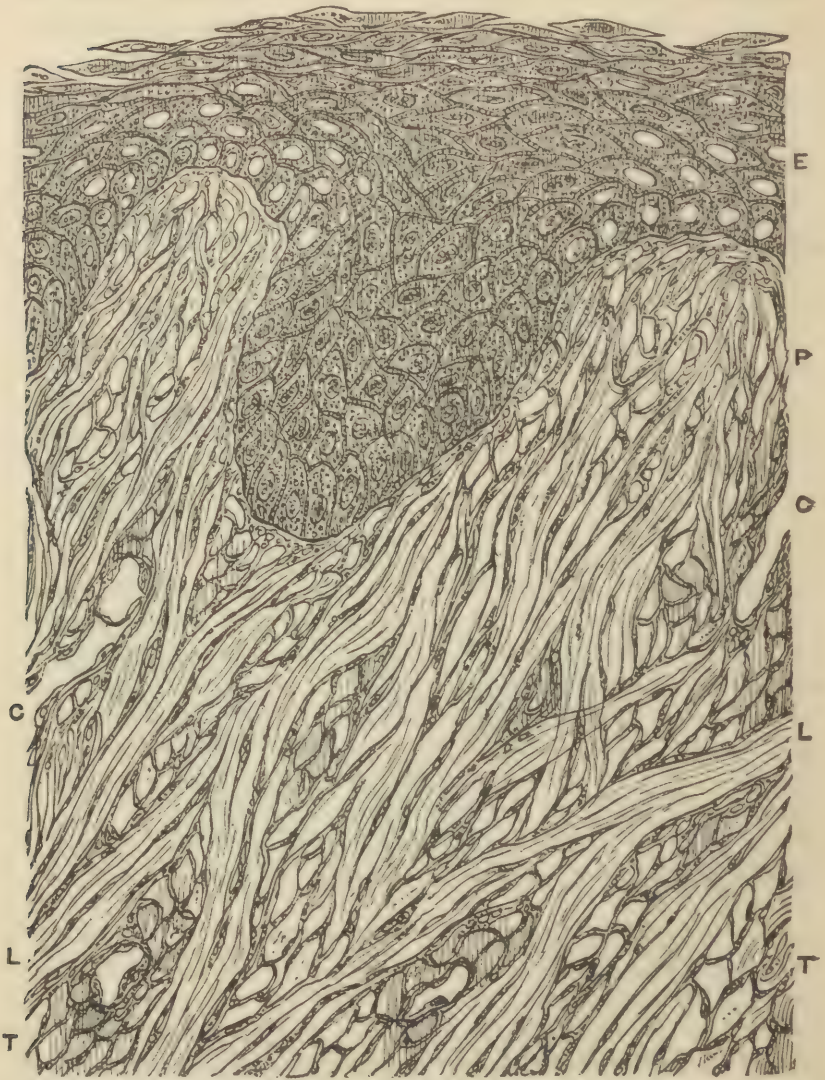

FIG. 4. Fibroma of the Alveolar Process of the Upper Jaw. E, Stratified epithelium of the gum; P, Blunt papillæ of the gum; L, L, Longitudinal; T, T, Transverse sections of bundles of fibrous connective tissue; C, C, Capillary blood-vessels. × 200.

cess of their absorption. The prevailing idea as to their significance is that they grow by coalescence of leucocytes or medullary corpuscles, from without into the cement or dentinal tissue, liquefying in

their way these tissues, and breaking them up. Hence their name, "osteoclasts," or "bone-breakers."

We must decidedly disagree with such views, since we have seen multinuclear protoplasmic bodies arising from the living matter of cementum and dentine itself, after the dissolution of the lime-salts, and the liquefaction of the basis-substance. We furthermore have often seen such bodies in the medulla, preceding the formation of bone-tissue. Since the territories of formed bone-tissue often are transformed into such multinuclear bodies, the idea becomes admissible that they can appear previous to development of the osseous territory; and to this view corresponds their presence in the periosteal portion of fibrous tumors. We admit, however, that this view does not account for the presence of so-called giant cells in every instance, since, as we will show later on, they accompany blood-vessels, and are known to exist in inflammatory products,—for instance, in tubercles.

The tumor before us appeared on the alveolar process of the upper jaw in the shape of a cessile nodule, the size of half a hickory-nut, in a youth about twenty years of age. (Fig. 4.)

The surface of the tumor looked comparatively smooth to the naked eye, whereas microscopical specimens show remnants of the papillæ of the gum, rather shallow and blunt, and some distance apart. The outer coating is made up of stratified epithelium, whose layers are noticeably diminished, probably owing to the pressure of the growth from within. The first row of columnar epithelia is well marked only in the valleys between the remnants of the papillæ, while on their summits the first row is composed of short columnæ, or rather cuboidal epithelia. In these places both the epithelia of the first and the neighboring epithelia of the adjacent layers exhibit central vacuoles, or plasmatic spaces, from which the nuclei have dropped out.

The bundles of the fibrous connective tissue are of considerable breadth throughout the mass of the tumor, but their breadth increases from the outer to the deeper portion. The protoplasmic tracts are well marked between the bundles, both in longitudinal and transverse sections. The bundles are freely decussating or interlacing, by which an extremely dense trestle-work, similar to that of the derma of the skin, is produced. The vessels are scanty throughout the tissue, consisting mainly of capillaries.

At the outer portion of the tumor, between the bundles, small nests of medullary tissue are discernible. The deepest portions, on the contrary, are made up largely of medullary tissue, composed of globular and spindle-shaped corpuscles, with a goodly number of interspersed multinuclear bodies. The latter feature does not mean a

transformation from the benign fibroma into a malignant myeloma, but the juvenile condition of the connective tissue, and a somewhat

Fig. 5.

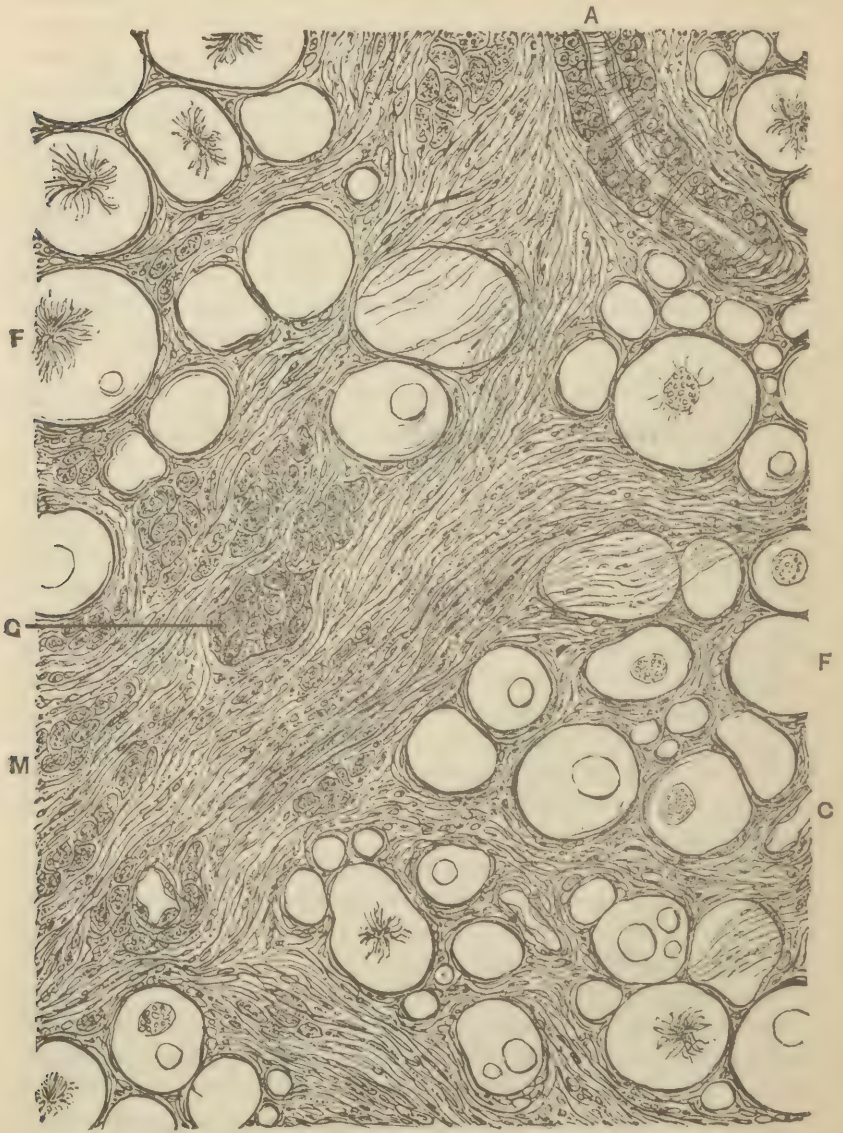

Fig. 5. Lipo-Fibroma of Lower Jaw. F, F, Fat-globules; M, Clusters of medullary corpuscles; G, Multinuclear body or giant cell; A, Artery. × 200.

accelerated growth from beneath. This is proven from the fact that the tumor did not return after removal.

IV.—Lipo-Fibroma.

In our collection there is no tumor from the jaws made up of fat to such an extent as to warrant a diagnosis of lipoma. One specimen, however, removed from the lower jaw, the size of a cherry, shows a combination of fibrous connective with fat tissue, and thus gives the variety expressed in the title. The fat-globules are greatly varying in size, and either arranged in groups or scattered singly in the connective tissue; arteries are accompanied by rows of such globules. Most of the latter contain vacuoles and peculiar star-shaped formations in their centers, which very probably are not crystals of margaric acid, as some previous observers have believed, but remnants of protoplasm, known to exist in each fat-globule. (See Fig. 5.)

The connective tissue is of two kinds, viz., partly broad and heavy bundles, and partly narrow spindles, not arranged in distinct bundles. These two varieties are intermixed without any regularity throughout the entire tumor, the latter being especially conspicuous in the neighborhood of the fat tissue, where it produces a thin layer, carrying blood-vessels between the fat-globules, or surrounds groups of them. The connective tissue contains a number of clusters of medullary corpuscles, which, if flattened out and rendered polyhedral by mutual pressure, present the aspect of endothelia, and if coalesced into one mass represent multinuclear bodies or giant cells. The history of development of fat tissue demonstrates that each globule of a larger size arises from a number of medullary corpuscles, which are transformed chemically into fat, whereas the central portions remain unchanged protoplasm, with branching offshoots; much on the plan of territories with central cartilage or bone-corpuscles. Small fat-globules may be the products of transformation of single medullary corpuscles, or a limited number thereof. It has long been known that, in animals in which emaciation is induced rapidly by starvation, each fat-globule breaks up into a number of medullary corpuscles,—viz., into the embryonal material which originally gave rise to the formation of a globule. If we recall the fact that each fat-globule is surrounded by a thin connective-tissue corpuscle, invariably supplied with a nucleus, fat at once appears as a variety of myxomatous tissue, the difference being only a chemical alteration of the protoplasm into carbohydrates or fat, instead of a mucoid basis-substance.

From this point of view, the clusters of medullary or endothelial corpuscles would simply represent a pre-stage of future fat-globules or remnants of previous ones. Since multinuclear bodies or giant cells are known to result from a coalescence of medullary or en-

dothelial corpuscles, there is good reason to assume that these bodies likewise would represent eventually either a previous or a past stage of fat-globules. A fat-globule, according to our view, is a globular territory with a central protoplasmic body, growing in exactly the same manner as a territory of myxomatous, cartilaginous, or osseous tissue; the nucleus always belonging to the capsule around the globule, and not to the globule itself. A territory of any of the named tissues will break up, in the process of physiological or reduction in pathological conditions, into clusters of medullary corpuscles, or into multinuclear protoplasmic bodies.

V.—Angioma.

A boy, eleven years of age, presented himself with a tumor the size of a small hickory-nut on the gum of the lower jaw, occupying the region of the right lateral incisor and cuspid, having its rise in a somewhat narrow pedicle between the teeth. The surface was nearly smooth, slightly lobulated; its consistence rather soft, and easily compressible; its color dark-red. Pressure with the finger rendered the tumor pale, considerably diminishing its bulk at the same time, but as soon as the pressure ceased the previous size and color returned. Three months previously a similar tumor had been removed from the same place, but it almost immediately commenced to grow again with alarming rapidity, causing a slightly uneasy feeling, but no pain.

Vertical sections through the body of the tumor revealed the fact that its interior was composed mainly of blood-vessels, but that it was different in its structure in the outer and inner portions. The former exhibited the features of a lobular, the latter of a cavernous, angioma.

A, Lobular Angioma.—The surface of the vascular or erectile tumor is covered with a stratified epithelium, being normal in its breadth at the borders, and much thinned in the middle portions of the tumor. In the former places there are visible numerous rather shallow papillæ, a certain number of which are united into a group by deep epithelial valleys. In the central portions only a limited number of layers of cuboidal epithelia are discernible, the deepest layer being absent, and replaced by medullary corpuscles to such an extent that no boundary line could be made out between the epithelium and the subjacent connective tissue. (See Fig. 6.)

The connective-tissue layer beneath the epithelium is made up of nucleated granular corpuscles, closely packed together,—so much so that they flatten each other into broad spindles. Bodies of this description are termed endothelia. A limited number of tumors of this variety are known since Bizzoziro, of Italy, drew attention to

their occurrence, and dubbed them endothelioma. They are mainly in connection with lipoma and angioma.

FIG. 6.

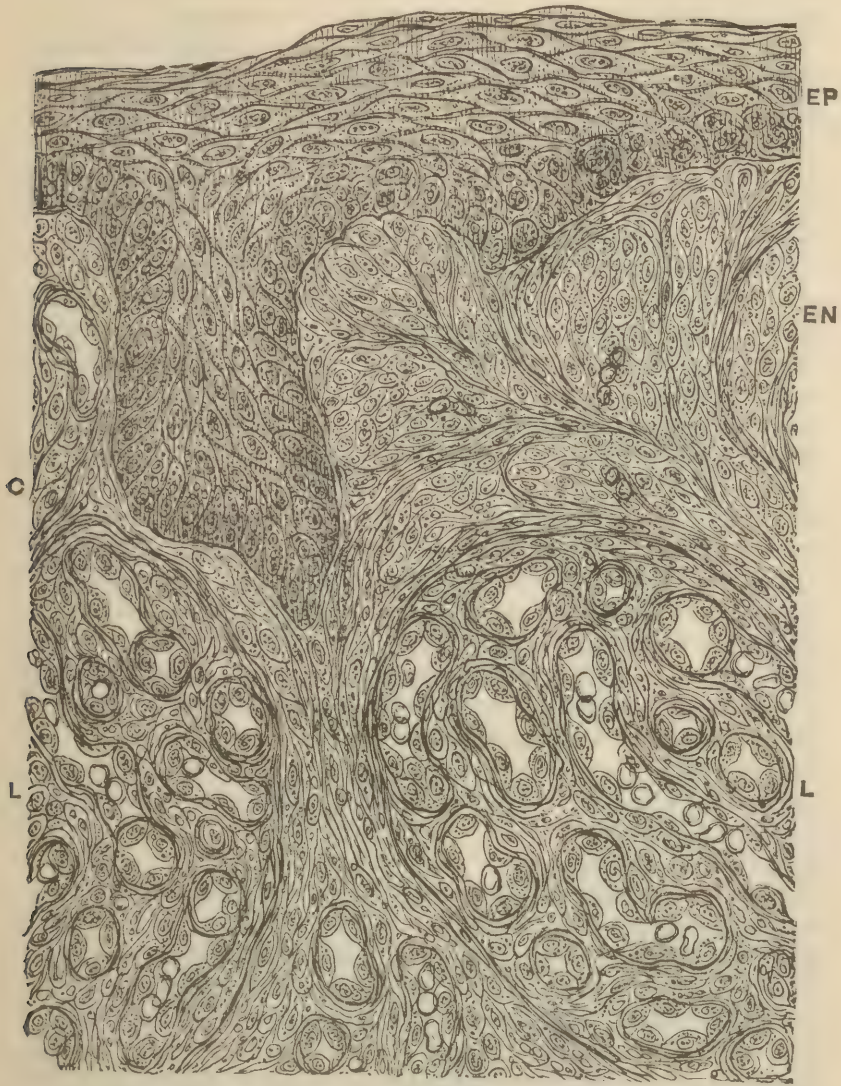

FIG. 6. Lobular Angioma of the Gum of the Lower Jaw. E, P, Stratified epithelium whose columnar epithelia toward the right side are breaking up into medullary corpuscles. EN, Endothelial layer traversed by radiating tracts of a delicate fibrous connective tissue; C, Capillary blood-vessels in the endothelial layer; L, L, Lobules composed mainly of capillary blood-vessels. × 200.

The endothelia appear to be arranged in clusters, between which delicate tracts of a fibrous connective tissue run in a somewhat radiating order, which tracts, if viewed with higher powers of the

microscope, appear to be made up of narrow, partly-nucleated spindles. The tracts spread towards the periphery in a fan shape, and no clear distinction is possible here between the broad spindles of the endothelia and the narrow spindles of the tracts.

Some distance below the epithelia, or close beneath them, a large number of capillaries are seen cut in longitudinal, oblique, and transverse sections, which means that these blood-vessels are coiled up into a lobular shape. Between the lobules there are either tracts of endothelia mixed with fibrous connective tissue or bundles of the latter alone, and these interstitial tracts bear capillaries of their own, independently of those within the lobules.

The most striking feature in the endothelial layers is the formation of red-blood corpuscles and blood-vessels. At first isolated lumps appear in the endothelia, characterized by a high degree of refraction, and yellow in color. They are smaller than red-blood corpuscles, and are known by the name of "hæmatoblasts." Increasing in size, they assume the appearance and structure of red-blood corpuscles. Clusters of hæmatoblasts, or fully-formed red-blood corpuscles, are surrounded by circular tracts of endothelia, which, being hollowed out in part, lead to the formation of calibers already filled with blood, whereas a number of endothelia of rather large size furnish the walls of the capillaries. Thus the formation of red-blood corpuscles precedes that of blood-vessels, as stated some forty-five years ago by the late Rokitansky, of Vienna. Thus it also becomes plain that the tissue form termed endothelioma is, at least in many instances, a pre-stage of angioma. Obviously the newly-formed blood-vessels, though containing blood-corpuscles from the very issue, are closed tubes or sacules, which later, through a continued vacuolation of the endothelia, inosculate with already formed blood-vessels; their tenants, the blood-corpuscles, entering into circulation.

B, Cavernous Angioma.—The lower portions of the tumor under consideration have a different structure, gradually blending with that of lobular angioma. Here we notice large cavities, at first lined by several layers of endothelia, and containing a varying number of red-blood corpuscles, until at last very large spaces make their appearance, filled with red-blood corpuscles; and thus the character of a cavernous angioma is established. (See Fig. 7.)

We observe, at first, tracts of endothelia accompanied by a delicate fibrous connective tissue, with irregular calibers, in which a liquefaction of a certain number has taken place, as indicated by their hydropic condition, to such an extent that only a delicate frame-work of previous endothelia is discernible. A certain number of endothelia have been transformed into red-blood corpuscles;

another set furnishes colorless blood-corpuscles, or possibly these arise from the nuclei of previous endothelia. This process is known to

FIG. 7.

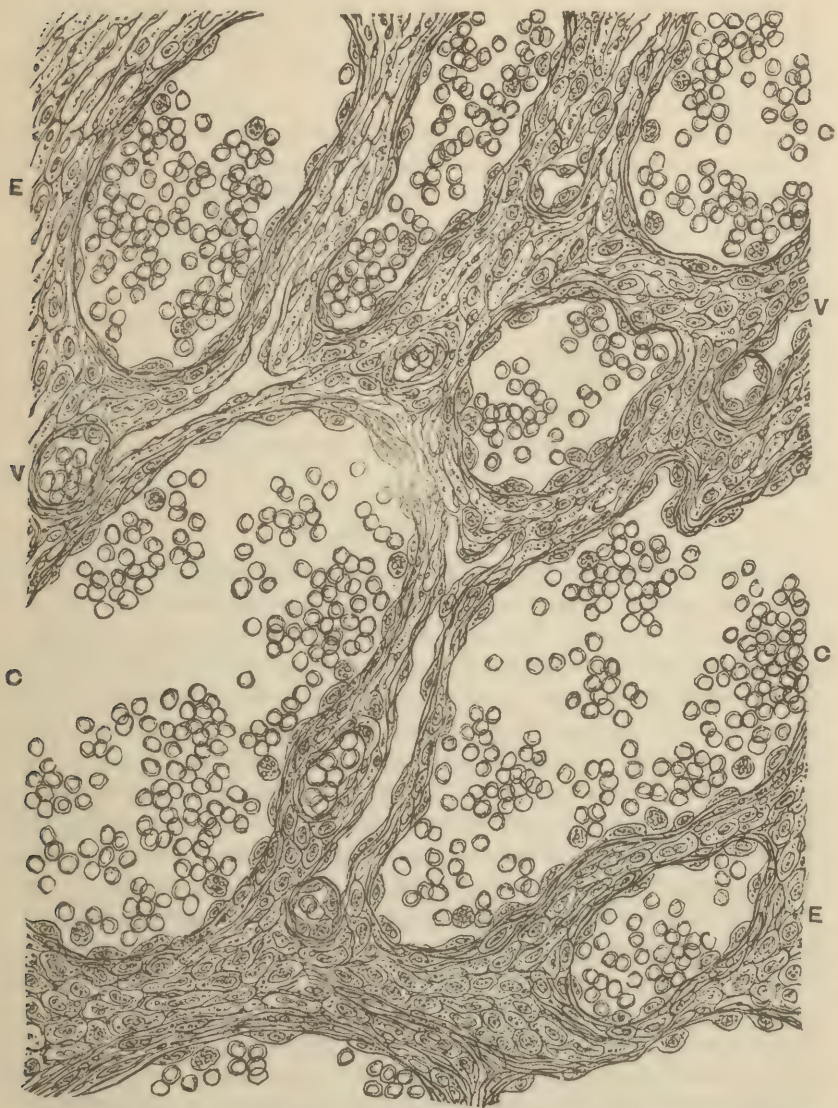

FIG. 7. Cavernous Angioma from the Base of a Vascular Tumor of the Gum. C, C, Cavernous spaces filled with venous blood; V, V, Capillary blood-vessels of the trabeculæ bounding the cavities; E, E, Endothelia in transition, partly into myxomatous and partly into fibrous connective tissue. × 200.

histologists by the term of "vacuolation of the endothelia." The calibers at first are very irregular, being bounded by several layers

of endothelia, and it sometimes occurs that tolerably well-formed calibers of the same vessel are connected with one another by narrow canals, owing to the presence of little changed endothelia. Blood-corpuscles may be seen in one part of the caliber, and are absent in another, so long as the vessels are not complete. The remaining endothelia are large and supplied with oblong nuclei of considerable size.

Fully-formed cavities in connection with the physiological vessels are characterized by smaller endothelia, not surpassing in size those of normal veins. The trabeculæ inclosing the venous cavities are made up of fibrous connective tissue, carrying their own capillary blood-vessels. In many places, however, even the trabeculæ are made up of endothelia, and it is easy of demonstration that the endothelia are merely the medullary or embryonal stage of connective tissue, since we can trace its transformation both into myxomatous and fibrous connective tissue. This portion of the tumor contains solid masses of a dense fibrous connective tissue, which in all probability are not newly formed, but represent residues of the former tissue of the gum or the periosteum.

VI.—Myeloma.

In the introduction we have given the reasons why we prefer the term myeloma to that of sarcoma. These tumors are by no means of rare occurrence, as shown by our comparatively small collection, which embraces five specimens of myeloma and its combinations out of seventeen representatives of tumors in general. All these tumors are considered malignant with but one exception, which concerns the variety termed "epulis sarcomatosa," or, as we propose to call it, fibro-myeloma. This variety is well-known to surgeons as admitting of a radical cure if thoroughly extirpated. Multinuclear bodies are of such frequent occurrence that an authority like Virchow speaks of a variety which he calls "giant-cell sarcoma," growing in the majority of cases from the periosteum. We have described, under a previous heading, benign tumors, especially fibroma, containing a varying number of so-called giant cells in their juvenile portions, where medullary tissue prevails, and we have emphasized that no stress is to be laid upon the presence of "giant cells." If the tumor is intermixed with medullary tissue throughout, the diagnosis will be fibro-myeloma, which is still of a low degree of malignity, as shown by clinical experience. We can state positively that the number of multinuclear bodies is of great value for determining the degree of malignity in any given case. The greater their number the surer it is that the tumor is not very malignant, and will not recur if radically removed. On the contrary, the smaller their number

the greater is the malignity and the danger of recurrence; whereas, in the worst cases of pure globo or spindle myeloma, multinuclear bodies are lacking altogether. In such cases the danger to the life of the patient is imminent, in spite of all attempts at thorough eradication.

According to our nomenclature, we will dwell upon combinations such as myxo, fibro, and osteo-myeloma, and at last consider the two purely malignant forms,—viz., globo and spindle myeloma. Either of these forms may arise primarily from the periosteum or medulla of the jaw-bones, or start in the nasal cavity, the antrum of Highmore, or the soft palate, and invade the upper jaw in a secondary manner. In several instances of primary myeloma we found, in the tissue of the tumor, clusters of pigment indicative of a previous hemorrhage, possibly in connection with a traumatism (blow, kick, fall, etc.), which, as is admitted, often causes—for reasons unknown —the growth of malignant tumors.

A, Myxo-Myeloma.—This specimen originally started on the soft palate of a young lady near twenty years of age, and after extirpation recurred on the base of the upper jaw-bone, invading in turn both the antrum and the nasal cavities. With low powers of the microscope the tumor shows a thin investment of fibrous connective tissue, fibers from which penetrate the morbid growth, scantily supplied with blood-vessels, and producing imperfect septa, by which an indistinct alveolar structure results. The alveoli are filled with protoplasmic bodies, either globular or spindle-shaped, or provided with numerous offshoots, by means of which a net-like structure is established. (See Fig. 8.)

Globular corpuscles are arranged in clusters, with a scanty intervening basis-substance. Spindle-shaped corpuscles are arranged in tracts, freely connecting at acute angles, and separated from one another by a slight amount of a finely-granular basis-substance. This latter form would correspond to that variety of myeloma termed by Virchow "net-cell sarcoma." The prevailing formation within the alveoli, however, corresponds to the illustration, being composed of very large polymorphous protoplasmic masses, partly containing a number of nuclei, and interconnected by comparatively narrow offshoots in all directions. The basis-substance between these formations is conspicuous, and traversed by an extremely delicate reticulum, which arises from the delicate offshoots in a brush-like manner. This tissue in structure is myxomatous, and being in predominance over the structures before mentioned, entitles the tumor to the name of myxo-myeloma. The myxomatous tissue contains no blood-vessels, which invariably run in tracts of fibrous connective tissue, at rather distant intervals. As the consistence of the

tumor was soft, almost jelly-like, the basis-substance must be of the mucoid or myxomatous variety. In cases where the basis-substance is more firm the tumor has been termed chondro-myeloma, or malignant chondroma, although we would consider the latter term as illogical.

B, Fibro-Myeloma.—Among several tumors of this variety, we have selected the present specimen for description, its clinical history

FIG. 8.

FIG. 8. Myxo-Myeloma of Upper Jaw filling the Antrum of Highmore. F, Tract of fibrous connective tissue; V, Capillary blood-vessel; S, S, Nucleated protoplasmic tracts branching and finely interconnecting; B, B, Myxomatous basis-substance with a delicate reticulum in connection with the protoplasmic bodies. × 600.

being better known. It was located upon the right side of the lower jaw of a man about thirty-five years of age, the size of half a hen's-egg, occupying a space between the first bicuspid and the ramus; the teeth in this situation having previously been removed. Its consistence was firm, its surface slightly nodular, its color purple, and there were nowhere signs of ulceration. For a while previous

to its removal it caused considerable pain of a shooting character. It had grown within about two years.

Fig. 9.

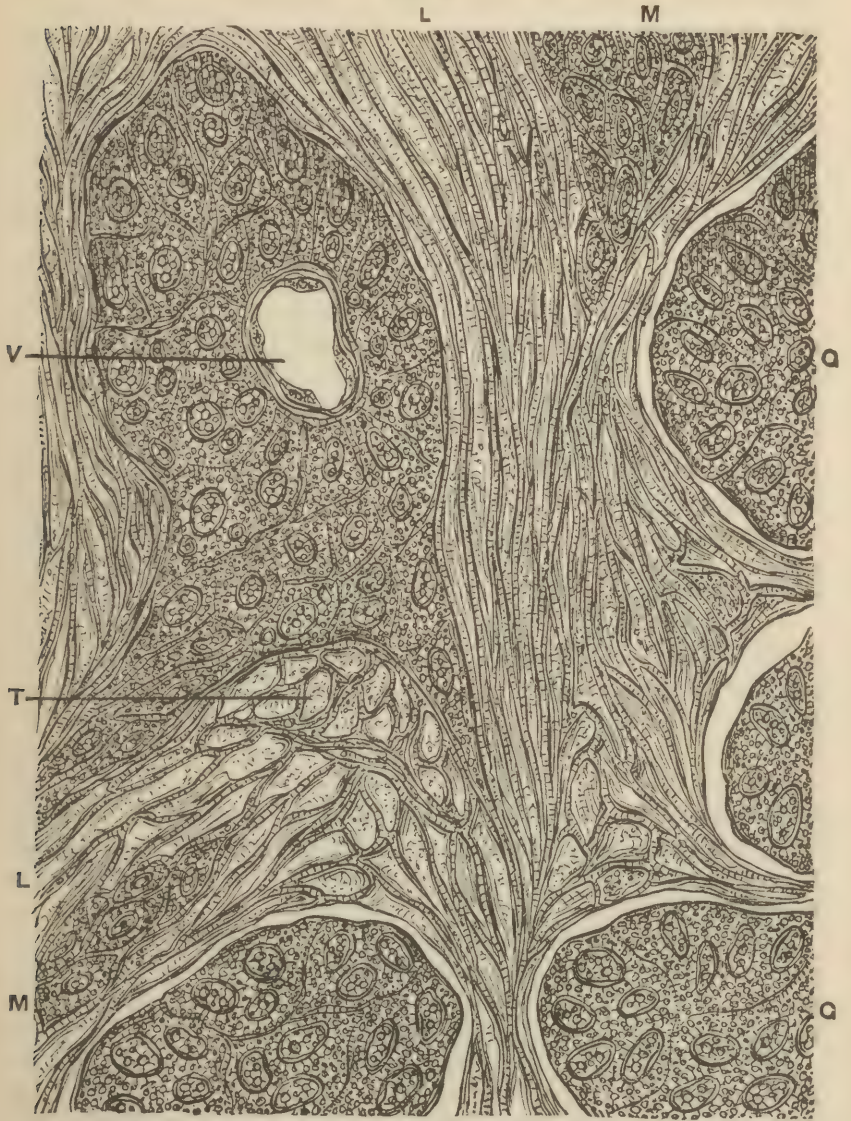

Fig 9. Fibro-Myeloma with Multinuclear Bodies from the Lower Jaw. L, L, Longitudinal; T, Transverse sections of bundles of fibrous connective tissue; M, M, Clusters of medullary corpuscles; G, G, Multinuclear bodies or so-called giant cells, retracted from the adjacent connective tissue; V, Blood-vessel in transverse section surrounding a cluster of medullary corpuscles. × 600.

Under the microscope the tumor appears to be composed of interlacing tracts of fibrous connective tissue, with interstices filled either

with medullary corpuscles or with multinuclear protoplasmic bodies; the fibrous portion everywhere being in excess over the medullary tissue. (Fig. 9.) The clusters of medullary corpuscles were rather numerous, exhibiting an endothelial appearance. In some places blood-vessels are seen to be surrounded with or accompanied by such medullary corpuscles, and in a few places multinuclear bodies are visible in small numbers; but in a remarkably regular arrangment. The fact that blood-vessels traverse the clusters excludes their being of an epithelial nature, and therefore the diagnosis of cancer, which could be made upon a superficial glance at the tumor, is untenable. This tumor we would not consider a very maligant one, and the diagnosis of a fibroma would be admissible if the medullary nests were not so profusely scattered throughout the tissue.

A far more malignant case of fibro-myeloma is the following: A man about twenty-five years of age showed a hard swelling upon the right upper maxilla, which had developed within three years. The tumor occupied not only the region of the alveolar process, but also the antrum of Highmore. Most of the teeth became loose and had been removed, the two last molars being left, but very loose, and nearly imbedded in the dark-red mass of the tumor. The diagnosis was malignant tumor, either cancer or myeloma. The whole right maxilla was extirpated, and a portion of the alveolar process with a tooth in it came into our possession.

At the microscopical examination no trace of a bony structure could be found; the mass of the tumor consisting mainly of clusters of small globular shining corpuscles, between which an indistinct fibrous reticulum was discernible. The clusters were separated from each other by bundles of fibrous connective tissue, greatly varying in amount; the surface of the tumor was bordered by an indistinct capsule of the same tissue, which itself contained smaller clusters of myeloma corpuscles, and showed irregular, blunt elevations belonging to the gum, and covered with a thin layer of stratified epithelium.

In the neighborhood of the tooth the pericementum was still recognizable, in the shape of straight bundles of fibrous connective tissue, still in connection with the cementum, but crowded with myeloma corpuscles. (See Fig. 10.)

In this situation it is evident that the tissue of the myeloma grew at the expense of the fibrous connective tissue of the pericementum. In some places the bundles of the latter tissue are still broad, containing in their middle slit-like groups of medullary corpuscles. In other places these corpuscles have replaced the bundles to a great extent; still further, only scanty and thin bundles are seen traversing the tissue of the myeloma. At the last elements of myeloma oc-

cupy large fields, with scanty or no fibrous tissue between them. Obviously the process of transformation is explicable only if we admit that the whole of the fibrous connective tissue, the protoplasmic

Fig. 10.

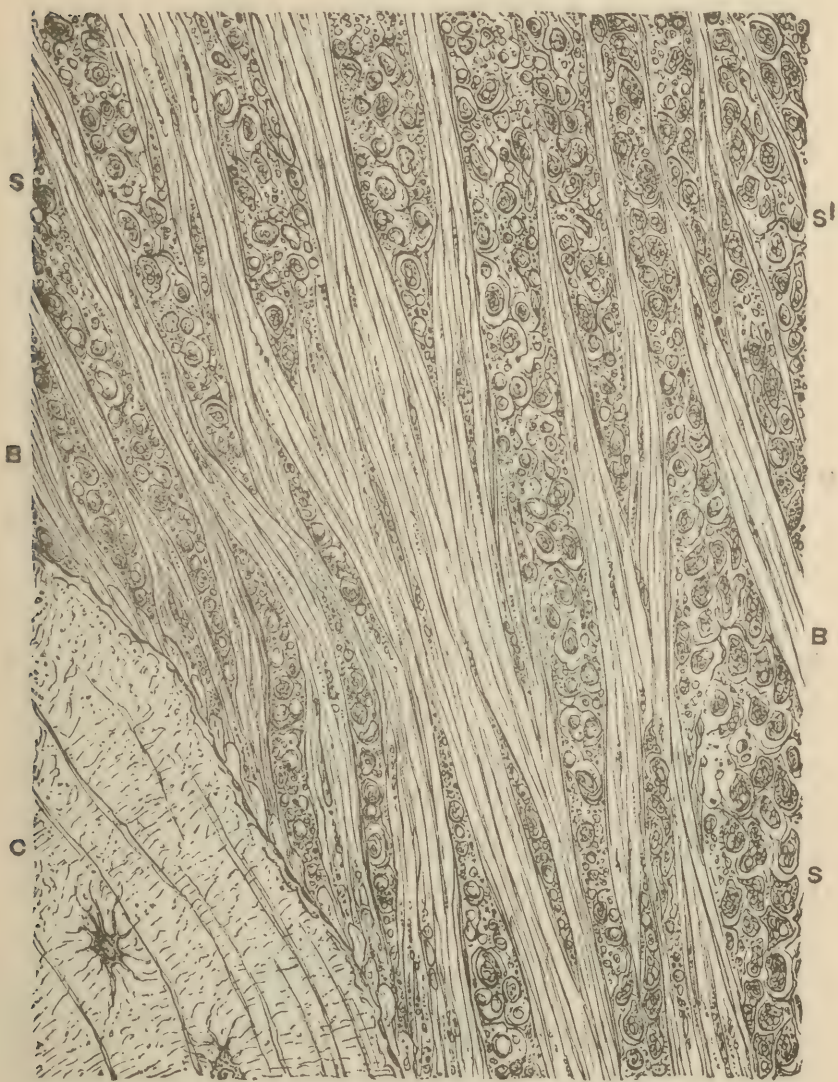

Fig. 10. Fibro-Myeloma of the Upper Jaw invading the Pericementum. C, Cementum; B, B, Bundles of fibrous connective tissue; S, S, Clusters of myeloma corpuscles between the bundles; S 1, Transformation of the bundles into the tissue of myeloma, with scanty traces of the bundles. × 200.

bodies as well as the basis-substance, is supplied with living matter, from which the new formation of the medullary corpuscles takes its origin.

If we confine ourselves to the examination of a limited portion of this tumor, no differentiation between myeloma and an acute inflam-

Fig. 11.

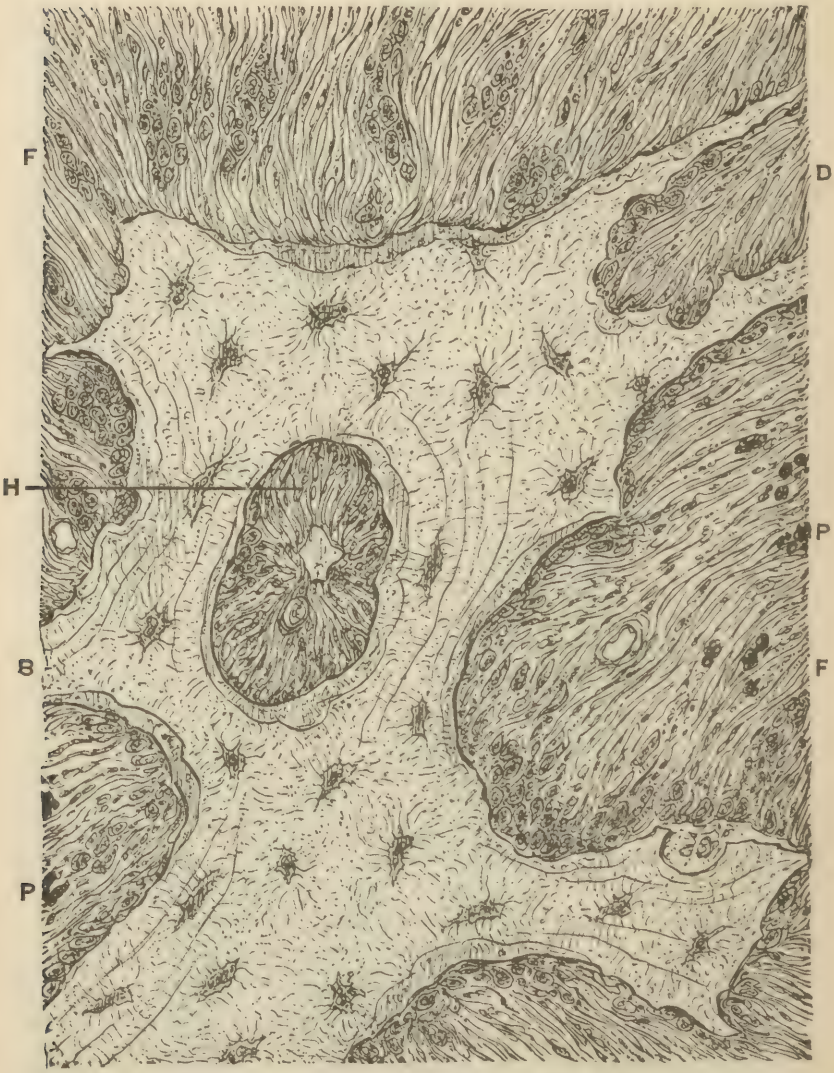

Fig. 11. Osteo-Fibro-Myeloma of the Alveolar Process of the Upper Jaw. F, F, Fibrous connective tissue with numerous clusters of medullary corpuscles; P, P, Clusters of pigment granules; B, Trabeculæ of bone indistinctly lamellated with normal bone-corpuscles; H, Medullary space with central blood-vessels; D, Bay-like excavation of the bone. × 200.

matory process can be made out, since the medullary corpuscles constituting myeloma are identical with inflammatory corpuscles

about ready to break up into pus. It should also be borne in mind that a rapidly-growing cancer may change its character into that of a myeloma, or fibro-myeloma, as first stated by Virchow. In specimens of such rapidly-growing tumors we have always to keep a sharp lookout for epithelial nests, the presence of which would be evidence of cancer. Should such nests be absent, we diagnosticate myeloma. We are, however, aware that either of these tumors involves considerable danger to the life of the patient.

C, Osteo-Myeloma.—This tumor was found in the mouth of a lady aged about thirty, in the region of the bicuspids upon the left upper jaw, and had reached the size of half a robin's-egg in a year and a half, the teeth having previously been removed. The tumor exhibited the structure of a fibro-myeloma, invading mainly the alveolar process, which was reduced to minute remnants of bone scattered throughout the tissue. (See Fig 11.)

The term osteo-myeloma is confined to growths primarily arising in the medulla of bone, or to growths holding newly-formed bone-tissue. As the tumor in this instance started in the medulla of the aveolar process, and is largely intermixed with fibrous connective tissue, its proper title would be osteo-fibro-myeloma. The remnants of bone-tissue give evidence of its transformation into the mass of the tumor through the intervening stage of medullary tissue. In a few places we find near the border of trabeculæ enlarged lacunæ containing several medullary corpuscles, obviously sprung from previous bone-corpuscles, and still surrounded by a calcified basis-substance. In other places a number of bone-corpuscles are seen connected by means of broad offshoots into chains. In still others, the first step toward the dissolution of the bone-tissue is the appearance of bay-like excavations corresponding to a previous territory, in which protoplasm makes its appearance; or the border of the bone is split up into a number of medullary corpuscles, which are not yet entirely freed from basis-substance. All this is strong proof that the bone actively participates in the new formation of the morbid tissue, the same as it participates in the process of inflammation. To say, as some authors do, that the bone is simply eaten up from without by the newly-formed tissue, does not prove much acuteness of observation; since it is by no means difficult to satisfy one's self as to the active proliferation of the bone-corpuscles within the lacunæ. It is invariably the medullary corpuscles that first appear from bone-tissue, and by subsequent splitting into spindles and reinfiltration with basis-substance give rise to the fibrous portion of the morbid growth.

D, Globo-Myeloma.—This specimen was obtained from a tumor taken from the mouth of a young lady about twenty years of age

It was located on the right upper jaw, in the region of the bicuspids, and had grown to the size of half an English walnut in about two years. The teeth had previously been removed. It was diffusely infiltrated toward the neighboring tissue, and evidently started from the periosteum. (See Fig. 12.)

The most striking feature was the scarcity of fibrous connective tissue, which in delicate bundles traverses the growth without any regularity. The main mass is composed of medullary corpuscles, either globular or polygonal, the latter produced by mutual pressure. Between small groups of such corpuscles extremely delicate septa of fibrous tissue are visible, in which the blood-vessels are located; though present only in small numbers.

Higher powers reveal two facts,—viz., first, that the corpuscles are interconnected by delicate radiating offshoots, traversing the nar-

Fig. 12.

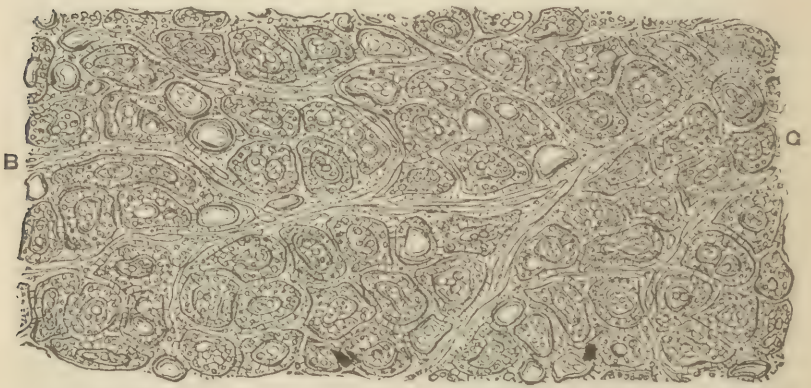

Fig. 12. Globo-Myeloma of the Periosteum of the Alveolar Process of the Upper Jaw. B, Delicate bundles of fibrous connective tissue; G, Globular corpuscles of myeloma in different stages of development. × 600.

row spaces between them; secondly, that in a limited field of the tissue all stages of development of myeloma can be made out.

We see small granules of a high refraction, structureless, not even reaching the size of colorless blood-corpuscles. We see larger granules and lumps with a varying number of vacuoles in their interior. We furthermore see lumps with large, compact nuclei, and at last corpuscles with reticulated nuclei, with granules in their interior, and of the ordinary recticulated structure of protoplasm. Any granule within the protoplasm may grow to the size of a nucleus, or a nucleated corpuscle; the nuclei themselves are in an active process of division, as shown by numerous dumb-bell forms, and figures of double or treble nuclei within a single corpuscle. All this is proof of a very rapid multiplication of the corpuscles, causing an ex-

tremely rapid growth of the tumor, and indicative of a high degree of malignancy. In accord with the latter features, not a single multinuclear body or "giant cell" can be seen, not even where somewhat broader bundles of fibrous tissue, probably belonging to the periosteum, are present.

E, Spindle Myeloma.—This tumor, corresponding to what Virchow has termed "spindle-cell sarcoma," is represented in our collection by a specimen the history of which is unknown to us. All we can say is that it had grown in the upper jaw. (See Fig 13.)

The tumor is largely composed of spindles, but in some places globular corpuscles are seen, which feature would entitle the tumor to the name of a combined globo-and-spindle myeloma. The tumor

FIG. 13.

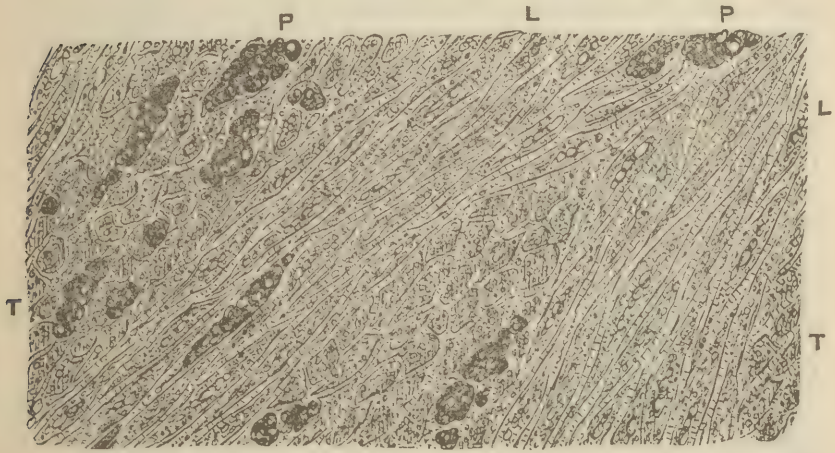

FIG. 13. Spindle-Myeloma of Upper Jaw. L, L, Longitudinal sections of spindles; T, T, Transverse sections of spindles; P, P, Clusters of pigment from previous hemorrhage. × 600.

has comparatively little of fibrous connective tissue, in which scanty blood-vessels are running. The spindles are arranged in interlacing groups,—so much so that in almost every field we meet with longitudinal and transverse sections of spindles, all of which are interconnected by delicate offshoots. The rapid growth of the tumor is indicated mainly by coarsely-granular nuclei, or chains of coarse granules, replacing the nuclei. In some places clusters of red-brown pigment granules are seen, but in such small numbers that the tumor cannot be properly called pigmented or melanotic myeloma. The pigment appears either in spindle-shaped or irregular clusters, partly within and partly between the spindle-shaped corpuscles. These pigment clusters are unquestionably the result of a previous hemorrhage, possibly caused by a mechanical injury, giving issue to the myelomatous new growth.

VII.—Carcinoma.

This type of tumors is characterized by the presence of epithelial nests, scattered without regularity in the connective tissue, which may be either myxomatous or fibrous. Most pathologists claim that cancer may orginate only in such tissues as are covered with or contain normal epithelia. The mucosa of both the oral and nasal cavities is the starting-point of cancerous growths, and in the upper jaw there is an additional source in the mucosa of the antrum. Again, the cancer may be primary in the tissue just named, or secondary by invasion from the skin or any glandular formation,—for instance, from the salivary glands.

There are three varities of cancer recognized by modern pathologists,—viz., first, scirrhous, with comparatively small nests of ephthelia, and a large amount of fibrous connective tissue around the nests; second, epithelioma, with concentrically arranged flat epithelia filling the nests, and a varying amount of fibrous tissue between them; and, third, medullary cancer, with small and irregular epithelia in the nests, and a scanty fibrous tissue between them. Of these three varieties our collection has two,—viz., epithelioma and medullary cancer, both having reached the upper jaw from adjacent epithelial structures, skin and mucous membrane.

A, *Epithelioma*.—We have two cases of this type of cancer, both from men over forty years of age. In one the tumor arose in the mucosa of the antrum, and in the other in that of the floor of the nasal cavity, both being similar in structure. (See Fig. 14.)

In viewing a specimen of epithelioma from the mucosa of the antrum, we observe marked differences in the structure of the epithelia. Near the boundary toward the connective tissue they are smaller and narrower than in the middle portions of the nests. They are often replaced by a row of medullary corpuscles, to such an extent that no sharp boundary line exists between the connective tissue and the epithelial nest. This obviously means a gradual transformation of the medullary into epithelial tissue, a process which leads to the increase of the bulk of the nests and a decrease of that of the connective tissue. At last, even the blood-vessels being obliterated, the nests are deprived of nourishing material, and a local necrosis—viz., ulceration—takes place, which is a common feature in all cancers.

The second prominent feature is an active new formation of living matter in the epithelia. This causes the nuclei to become homogeneous; then assuming an hour-glass shape, and lastly a division into several nuclei. Not infrequently we see several nuclei or several medullary corpuscles within a considerably enlarged epithelium. Such formations have been termed "mother cells" by previous path-

ologists, whereas to-day we know that they are the outcome of an active endogenous new formation. Around the nucleus often are

Fig. 14.

Fig. 14. Epithelioma of the Mucosa of the Antrum. C, Delicate fibrous connective tissue crowded with medullary corpuscles ; V, Capillary blood-vessels in the connective tissue; E, E, Epithelial nests made up of concentrically arranged flat epithelia; P, P, Cancer-pearls composed of changed epithelia. × 200.

seen vacuoles, or plasmatic spaces, which evidently contain nourishing liquid, enabling the nucleus to rapidly increase its amount of

living matter, with the result of fission and division, with a rapid new formation of epithelia. Except where the nucleus is surrounded by a vacuole, it is in connection with the adjacent protoplasm of the epithelium, by means of delicate conical offshoots. Similar offshoots also traverse the cement-substance between the epithelia, thus uniting all into a continuous mass of protoplasm. The central portions of the nests often contain groups of epithelia, which have assumed a high degree of refraction, a yellowish color, and a homogeneous appearance. At first the nuclei remain, though faintly discernible; but in the more advanced degrees of this metamorphosis even the traces of nuclei are lost, and a certain number of epithelia are transformed into structureless glistening plugs, representing the well-known cancer-pearls. The nature of this process is not yet known.

The connective tissue is either of the myxomatous or fibrous variety; never very rich in blood-vessels; mainly capillaries and veins. In many places the connective tissue is crowded with medullary or lymph-corpuscles, between which a delicate reticulum is seen. Some authors claim that this is the result of an inflammatory reaction of the epithelial upon the connective tissue, whereas we claim that it is the medullary condition of the connective tissue from which new epithelia arise. We base our views upon direct observation, since we know that if, after removal of cancer-nests, lymph-corpuscles be left behind, even though at a great distance from the cancer itself, the disease will invariably recur. This fact urges upon us the necessity for removal of large portions of tissue in the neighborhood of cancer. Modern surgeons, by clinical experience, have reached the same conclusion, which they consider the only safeguard again relapses, so very common in this disease. Unfortunately, we are not able to, say why the lymph-corpuscles or the medullary tissue, into which the connective tissue is transformed in an almost identical way with inflammatory infiltration, should have such a marked capacity for changing into epithelia; in other words, wherein the contagion of the tissue lies.

B, Medullary Cancer.—Our specimen is taken from the enormously enlarged alveolar process of the upper jaw of a man over sixty years of age. Twelve years previous to his death he was first operated upon for a so-called rodent ulcer, upon the left wing of the nose, which about fifteen years previously had orginated from a slight injury, causing a shallow ulcer, which could never be induced to heal. The scooped-out particles of tissue from the first operation were examined under the microscope, and showed the structure of a shallow or flat epithelioma, which previous authors termed "rodent ulcer."

Repeated recurrences and operations took place afterwards, until

the left upper jaw began to swell, the left eye was pushed up and forward, and the teeth became so loose and troublesome that they had to be removed. The swelling of the face proved to be greatly augmented by an apparently long-standing abscess in the antrum, the result of the death of a second molar many years before, the roots of which penetrated its floor. Upon the removal of this tooth a large

FIG. 15.

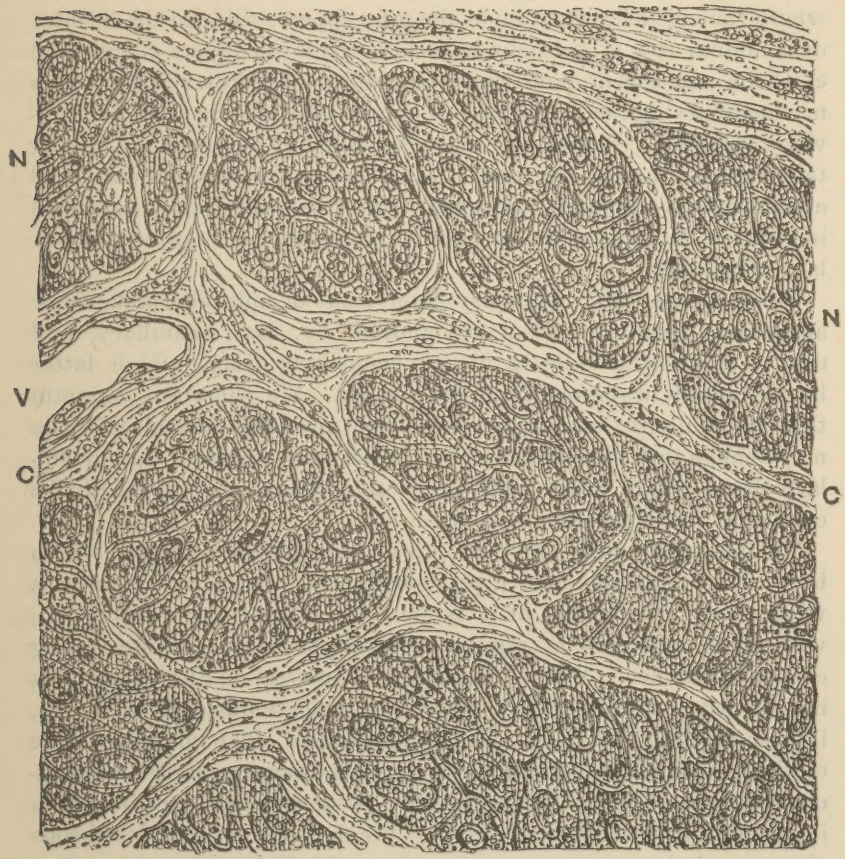

FIG. 15. Medullary Cancer of the Left Upper Jaw, invading the Alveolar Process and Gum. N, N, Nests of irregular polyhedral epithelia; C, C, Delicate fibrous connective tissue between the nests V, Vein. × 600.

quantity of fetid pus escaped, and a temporary improvement was the result. Later the swelling invaded the front of the mouth and passed to the right side to such a degree that several operations were required to remove the fungoid, easily-bleeding masses of the alveolar process, gum, and hard palate, which were almost choking the patient. The purpose of these operations was not to remove the

cancer, but to prevent death from suffocation or starvation. This specimen is a type of medullary cancer. (See Fig. 15.)

The specimen exhibited in some places an almost unchanged stratified epithelium covering the papillæ of the gum. In other places the papillæ were much enlarged and flattened. Still further, the papillæ have entirely disappeared and the epithelial layer is considerably thinned, until at last the epithelium had disappeared, and an ulcerating cancer-tissue appeared upon the surface. In those places where the epithelial stratum of the gum appears thinned the deepest or columnar row of epithelia as well as the lower layers of cuboidal epithelia are absent, and are replaced by a medullary tissue of a myxomatous character, which has incidentally sprung from the previous epithelia. We feel the more confident of such change having taken place from the fact that at the border between the epithelial and medullary tissues the epithelial bodies themselves show a marked increase of living matter, and a gradual transformation into medullary corpuscles.

Close beneath the medullary layer nests of epithelia make their appearance, separated from one another by, first, medullary, and deeper down by a delicate fibrous connective tissue, which latter has evidently orginated from the former. We therefore maintain that a medullary tissue which arose from previous normal epithelia may change into fibrous connective tissue, and *vice versa*, that medullary tissue which arose from connective tissue may eventually be converted into epithelia of cancer.

The medullary nests are made up of very irregular bodies, which by pressure have assumed a polygonal form. In many instances a whole nest or a portion of it is made up of granular protoplasm, with nuclei scattered at regular intervals, without any intervening cement-substance. Where the latter is present in the shape of a narrow ledge, it is invariably pierced by delicate offshoots or thorns, interconnecting the single epithelial elements. The changes of the epithelia toward proliferation are much the same as in the epithelioma before described. The connective tissue shows a transformation into lymph-tissue to a great extent. Where it has retained its fibrous character it is scanty, separating the epithelial nests and carrying a large number of protoplasmic bodies. The blood-vessels running therein are scanty, and prevailingly capillaries and veins. The latter often show sinuous contours, and are replete with blood-corpuscles. As stated under the heading of epithelioma, the secret of the general and local contagiousness of cancer has never been unveiled, but is left for future discovery.